

REPORT OF A SURVEY OF ACTIVE STUDIES IN GERONTOLOGY*

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Gerontology is the science of aging. All living matter ages from the moment of conception until death. Aging is a part of living and is thus involved in both evolutionary or growth phenomena and involutional processes. The aged and aging must not be confused. The aged are people; aging is a process. The aged are the consequences of this process. Thus gerontology differs from geriatrics in that the former is concerned with all the aspects of aging, whereas geriatrics is defined as "that branch of medical science which treats of the aged in their physiologic and pathologic relations."

Despite the obvious universality of the problems of aging, the science has been long and sadly neglected. The age of man as a species has received far more attention from anthropologists and archeologists than the aging of man as an individual or the basic mechanism of aging as

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a biologic phenomenon. It is only recently that these questions have aroused more than academic and theoretical interest. This is quickly changing. The near future will see an ever increasing concern with the problems of aging in all their many and complex ramifications. The conspicuous shift to greater average age and rising proportion of the elderly in the population make the study and solution of many of these questions a matter of true and serious urgency.

Preventive medicine, sanitation and vastly improved pediatrics have been responsible for the dramatic rise in longevity and life-expectancy through the prevention and better therapy of infective diseases. The trend of increase in average age continues and was, in fact, accelerated in the last decade.

In 1900 the average life expectancy at birth was but 47; today it exceeds 62 for the white races. (1) In 1900 only 17.8 percent of the total population of the United States were 45 or more years old. In 1940, as revealed by the preliminary studies of the 1940 Census, 26.5 percent were over 45. (2) The Census Bureau, assuming that there will be no net immigration, and that the present trends continue, predicts that in 1980, those of 45 and over will constitute 40.4 percent of the total population. (3)

Analysis of the data from the 1940 Census also reveals that the median age of the population of this country increased from 26.4 years in 1930 to 28.9 years in 1940. This is an increase of 2.5 years within a decade. Furthermore, the number of persons aged 65 or more increased from 6,633,805 to 8,956,206 in the ten years from 1930 to 1940. This constituted a rise of 35 percent among those of 65 or more in contrast to a 7.2 percent increase in the total population of the United States in this last decade. (2,4)

The implications of such facts are so vast that no apology is needed in emphasizing the importance of gerontology. The aged are here in unprecedented numbers; there are nearly nine million persons over 65 in the United States today. There will be many more of them in the years to come. These older men and women will remain an urgent problem until enough is known about aging to maintain health into senility and to employ wisely the changed capacities of those past the meridian of life. These questions are the immediate concern of everyone, as individuals or as parts of corporate industry, educational institutions or government, for either the increasing millions of elderly persons must have opportunity to work at tasks suited to their

capacities so they may support themselves and remain usefully productive citizens, or the proportionately dwindling group of younger people must support them in one way or another. (5) There are vast, though largely unappreciated and unutilized potentialities in the elderly. But, before these can be developed, industry and medicine must learn much more about the changed capacities of aging individuals (6) and educators must take cognizance of the need for adult education. (7) These are but two of the many unanswered questions clamoring for solution.

Were all these elderly people vigorous and well, the social and economic problems would be greatly simplified and there would be reason to rejoice complacently in the benefits of advancing medical science. (7) But they are not all healthy. A large and growing fraction suffer from the chronic, progressive, and disabling disorders characteristic of the years of later maturity. Men rarely age normally. The most significant so-called "degenerative disorders" are cardiovascular-renal disease, arthritis, diabetes mellitus, cancer, gout, and certain syndromes of the climacteric. Of all of these the cardiovascular group, including hypertensive arterial disease and arteriosclerosis, is by far the most significant. (8) The arthropathies exact an immense toll of disability, though their mortality is low. The economic

burden and medical problems of prevention, early diagnosis, and treatment of chronic diseases demand immediate attention.

(2,10)

The prophylactic aspects of geriatrics are of the greatest importance. They differ widely from those of preventive medicine for younger age groups. The diseases of youth are usually acute, self-limited and have florid onsets so that early identification is relatively easy. In contrast, the disorders most frequent in the later decades are chiefly chronic, progressive and insidious of onset. Thus early therapy is often neglected because of the absence of distress. At present many of these diseases are not amenable to cure. Control and/or retardation of progression are, however, feasible objectives. The earlier control measures are instituted and the more highly individualized those measures are, the more effective is preventive geriatrics. Senescence does not begin in the aged. If the progressive degenerative disorders can be detected and controlled before structural and functional damage becomes irrevocable, senescence will become a normal phenomenon and disablement may be long deferred.

Normal aging brings many changes. Normal is not a fixed point, but a series of variables which change with age. Accuracy in health measurement and in the detection

of the earliest manifestations of incipient disease depends upon recognition of these variables. Therefore, one of the most pressing tasks of clinical geriatrics is to define much more precisely than has been done heretofore just what the criteria of normality are in relation to age. Health is far more than the absence of disease. Health has quantitative attributes which involve reserve capacities. Extensive and carefully controlled research into the changes in these functional capacities and variations in "physiologic constants," such as the arterial tension, vascular elasticity, and concentrations of chemical constituents of the blood in relation to age are necessary for future accuracy in health mensuration.

There is a common misconception that senescence implies decline alone. This erroneous assumption has greatly retarded the development of the science of gerontology and has engendered a fatalistic inertia even among scientists. With aging certain capacities and attributes become enhanced; many of these increments are compensatory to depreciations in other capacities. For example, diminution of physical strength and speed of reaction are often largely counterbalanced by increased skill and judgment. Adaptation may be slowed, but sense of responsibility is enhanced. Wisdom is conditioned by experience, which, in turn, is a factor

of time, or age. Admittedly, aging does not create critical judgment. However, time fosters its growth when intelligence exists in youth and cultivation is continued. It is because of trained judgment, special knowledge and experience that the leaders carrying the gravest responsibilities in all walks of life are older men. The potentialities of development of the older mind by continued cultivation are as yet almost wholly unappreciated. (11) Extensive study of the methods and consequences of effective adult education should reveal much more of the immense, unutilized reservoir of constructive effort resident in the millions of elderly persons.

The vast problems of aging are so multifaceted and involve so many disciplines that to plan future research without orientation to the whole would invite sorry confusion, wasted effort, time and funds, and redundant duplication. The orchestration of research involves three preliminary steps: 1) The orientation of the categories of thought involved; 2) inventory of present and projected research studies; and 3) correlation of existing knowledge for the purpose of formulating a broad program of investigation.

The Problems of Gerontology

Gerontology is logically divided into three major categories and may be outlined briefly as follows:-

1. The Biology of Aging

1.1 The phenomena of evolution or development

1.2 The phenomena of involution or senescence

2. The Clinical Problems of Aging Man

2.1 Pediatrics

2.2 Geriatrics

2.21 Normal senescence and senility

2.211 Physical aspects

2.212 Mental aspects

2.22 Diseases of the Senescent Period

2.221 Physical disorders

2.222 Mental disorders

3. The Socio-economic Problems of Aging Mankind

3.1 National economic problems

3.11 Unemployment in relation to age

3.12 Chronic illness in and after maturity

3.13 Mental disease in senescents

3.2 Industrial problems of aging personnel

3.3 Cultural problems

This delineation of the problems of aging is, of necessity, highly condensed and presents merely the major skeletal divisions. Each part or section includes subdivisions too numerous to record here. These all present many unanswered questions in urgent need of elucidation. Theoretically, growth, development, differentiation, and maturation are just as much consequences of aging as are the involutional atrophies and metabolic changes of senescence, for the two groups of phenomena overlap and occur simultaneously throughout the life span. The present survey of investigations into gerontology, however, is concerned primarily with the later half of life, after full maturity. Thus pediatrics, although it rightfully fits into the science of gerontology, is deliberately omitted from any further discussion here.

The triad of primary categories which constitute the fundamental basis of gerontology are intimately and inseparably related, both pragmatically and theoretically. Though widely differing disciplines and techniques of scientific research may be applied in studies into the problems of aging, the observations and conclusions derived therefrom will still fit into this pattern and thus amplify the whole. Advances in any subdivision depend greatly upon parallel or preceding progress in other categories. It

cannot be over-emphasized that the more is known about the fundamental biologic mechanisms of the aging process, the more effectively can clinical medicine treat the aging and the aged. Likewise, the more comprehensive the clinical knowledge concerning the altering capacities and limitations of normal elderly persons and the prevention, control or retardation of the chronic and progressive disorders of later years, the more intelligently can the serious and complex social problems be attacked.

Procedure of Survey

The objectives of the present survey have been to determine, as thoroughly as was feasible, the directions of present and projected investigations into gerontology in the United States, and the scientific methods being employed. No inquiry has been made as to the results being derived from the many studies included; these will all be published by the investigators in good time. It was felt that compilation of such data should serve to assist in the formulation of future programs of research by avoiding unnecessary duplication as well as suggesting promising avenues of attack, and also aid in bringing together investigators studying related problems though applying widely differing disciplines. It has been deemed desirable that the Unit on Gerontology serve as a clearing

house and thought provoking agency. For obvious reasons the names of various investigators and the institutions involved are considered confidential.

The methods of obtaining data as to these questions included personal letters, publication of a request for information, and personal visits of inspection and conversation where the importance of the undertaking appeared to warrant it. A total of 677 personal letters of inquiry were mailed, including in the mailing list all those workers known to be interested in the problems of aging, deans of all medical schools in the United States (79), deans of agricultural colleges (42), deans of graduate schools and/or sociology departments in certain American universities (59), all those scientists suggested by the above academic executives, the directors of industrial health units in all the State health departments, many research institutes and foundations, the medical directors of 105 American railroads, a number of directors of industrial medical departments, and medical directors of those life insurance companies which were known to be interested in research. With each personal letter was enclosed the following resume' defining the purpose of the inquiry:

"The National Institute of Health of the United States Public Health Service is organizing a new unit for research into some of the many problems of aging. With the conspicuous shift to greater age in the population, senescent individuals are becoming increasingly significant in the national economy and defense. Preventive medicine must attack the practical problems of the rising proportion of deaths attributable to diseases of middle and later life and energetically attempt to augment the health and vigor of those past the meridian. Aging is a continuous biologic phenomenon which starts upon creation of a new individual and continues at variable rates until death. The problems of aging (gerontology) are not limited to the diseases of the aged (geriatrics), for the latter are the consequences of senescence. In man probably the most significant period of life for gerontologic study is late maturity, approximately the two decades between 40 and 60.

The problems of aging are logically divisible into three major fields of investigation: 1) the biology of senescence as a process, 2) the human clinical problems of aging and of diseases characteristically associated with advancing years which include the mental changes of senescence and senectitude as well as the physical changes, and 3) the socio-economic problems of a shifting age distribution in the population. The National Institute of Health is concerned with the first two of these divisions of the science.

In order to advise this new unit, there has been formed a National Advisory Committee on Gerontology, representative of the scientific thought of the Nation. The membership of this Advisory Committee includes:-

Dr. L. R. Thompson, Director, National Institute of Health, U. S. Public Health Service.
Dr. Anton J. Carlson, Physiologist, University of Chicago, National Research Council.
Dr. Charles L. Christiernin, Association of Life Insurance Medical Directors of America;
Medical Director, Metropolitan Life Insurance Company.

- Dr. Robert E. Coker, Zoologist, University of North Carolina.
- Dr. William Crocker, Botanist, Boyce Thompson Institute of Plant Research.
- Mr. Lawrence K. Frank, Sociologist, Josiah Macy, Jr. Foundation.
- Dr. A. Baird Hastings, Biochemist, Harvard University.
- Dr. Ludvig Hektoen, Pathologist; Consultant, National Cancer Institute, U. S. Public Health Service.
- Dr. Winfred Overholser, Psychiatrist; Superintendent, St. Elizabeths Hospital.
- Dr. Clarence Selby, Industrial Physician, General Motors Corporation.
- Dr. William D. Stroud, Clinician, Philadelphia.

The first service to scientific research which the Unit on Gerontology is undertaking is to conduct a survey of the present trends of active and contemplated investigations into the problems of aging in American scientific institutions. This survey is intended to ascertain just what problems are being studied and what methods of approach are being applied. There is no desire to learn, in advance of publication, the data being developed in these specific undertakings.

In addition to these studies, many investigations which do not pertain directly to aging should yield data useful to workers in gerontology. The Unit on Gerontology is especially interested in knowing of these indirectly related studies, the full implications of which are far too often obscured in their published titles.

Inquiries about studies related to aging are being sent to scientists in the basic sciences as well as to clinical investigators, for much fundamental work upon the processes, mechanisms and consequences of senescence is probably going on in the sciences of botany, zoology, physiology, pharmacology, psychology, etc. From the clinical viewpoint, our greatest concern is with those studies dealing with

health evaluation, mensuration of functional capacity (including criteria of "physiologic age") and with those diseases whose incidence increases sharply in later life (the so-called "degenerative disorders").

Critical analysis of the information elicited by such a survey may be expected to serve several valuable purposes. It should assist in bringing together in closer cooperation investigators interested in related problems, especially when widely divergent methods of approach are being utilized. The survey will likewise emphasize the urgent need for greatly augmented support for significant studies of these vitally important problems of senescence.

The broad and general pattern of the problems being investigated will undoubtedly reveal a number of neglected "blank spots" which may justify special emphasis in the future. Analysis of the data of the survey will also be an invaluable aid in formulating future research programs, both at the National Institute of Health and elsewhere.

From preliminary inquiries it is observed that there is a great but largely latent and scattered interest in the problems of aging. It is the hope of the Unit of Gerontology of the National Institute of Health that the present survey may serve to aid effectively the promotion of closer cooperation of the scientists interested in these fields.

Information concerning subjects under investigation and the methods of approach is earnestly solicited. Letters should be addressed to:

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The resume' was also sent to the editors of 53 scientific journals with a request for publication so that we could be reasonably sure that the mail inquiry missed no important workers. The response to the publication of this in about 25 journals was negligible, indicating that the more direct inquiries had reached almost all the investigators seriously interested in gerontologic research.

Correspondence revealed over 300 active or projected research studies pertaining to the problems of gerontology. Over two-thirds of our letters of inquiry were answered; the response early in the course of the survey was almost 100 percent, for then the correspondence was directed to workers known to be concerned in these fields. As previously mentioned, the publication of the resume' in many scientific journals failed to elicit any additional researches, though it did arouse interest and yielded several letters inquiring for further details.

The tone and character of the correspondence were almost uniformly cooperative. The Unit on Gerontology is extremely grateful for this splendid cooperation from its many correspondents; without such aid our efforts would been wholly futile. There was much enthusiasm in the responses from active workers; the great majority requested

that they be informed of the results of these inquiries. Particularly gratifying were the frequent indications that our letters and discussions aroused latent interest and have led to the initiation of a number of studies. Some of these will unquestionably prove noteworthy and significant.

Results of the Survey

Tabulation of the results of the survey is difficult because of the multiplicity of scientific disciplines involved and the many avenues of approach utilized. Classification of the studies first into the three major categories included in gerontology and then into more usual academic subdivisions of science appeared to be the most practical method of arrangement. Such organization permits of grouping studies by scientific methods. As the survey was intended to reveal objectives and methods rather than observations and conclusions, the present approach is appropriate. The clinical studies have been classified both by the specialty involved and by disease categories when the latter seemed the more feasible. It is inevitable that some overlapping occurs in classification, particularly where several scientific disciplines are being applied simultaneously. It is impossible to avoid a certain controversial arbitrariness in classifying some of the investigations.

1. Studies in the Biology of Senescence
(Biologic Sciences)

11. Genetics

- 11.1 Inbreeding experiments with rabbits notably changing the longevity of certain strains; one strain has been developed with a greatly shortened life span.
- 11.2 Study of the relation of genetics to longevity in rats by observation of two selected strains.
- 11.3 Relation of constitutional type to longevity in man, basing association upon structural type of scapula as found in various age groups.

12. Embryology

- 12.1 Study of the effects of aging of guinea pig and rat ova upon reproduction, viability and development. Ova aged before fertilization are prone to yield defective and abortive feti.
- 12.2 Interactions between cells and tissue fluids during embryonic morphogenesis; relation of organization to chemical equilibria as a factor of age.

13. Zoology

- 13.1 Study of the changes in tissue permeability and the deposition of calcium salts in relation to age in toads, planaria and other species.
- 13.2 Study of lactation during senescence in Jersey cows.

14. Botany

- 14.1 Study of the relation of the age of fruit trees to the size and character of the fruit borne.

- 14.2 Study of certain growth substances in stimulating dedifferentiation and re-differentiation in plants.
- 14.3 Relation of the increase in calcium in the cortex of cells in Elodea leaves with age. Study acquiring data which indicate that with aging the cells of these leaves become increasingly less permeable.
- 14.4 Chemistry of plant hormones and particularly the growth stimulating and growth retarding substances.
- 14.5 Temperature studies on ripening seeds in relation to age of seed.

15. Cellular Biology

- 15.1 Study of responses to stimuli to cell division in relation to age, applied to mammalian liver cells and measured by mitosis counts.
- 15.2 Study of the resistance of protozoa to drying in relation to age.
- 15.3 Tissue culture studies of responses to toxic agents in old and young tissue cultures.
- 15.4 Chemical study of the autolysis occurring during the involutional changes of metamorphosis of the bee moth (*Galleria mellonella*) larvae. Attempts at isolation of autolytic enzymes.
- 15.5 Mechanism of oxidation in embryonic cells in relation to age.
- 15.6 Correlation between temperature of environment and longevity, growth and reproduction in aphid *macrocyphum solanifolii*.
- 15.7 Oxidation-reduction potentials of tissues in relation to age.
- 15.8 Study of growth differentials by transplantation of organs at various ages and analysis of cellular and intercellular factors in salamander larvae.

- 15.9 Relation of osmotic concentrations of the body fluids with aging, using *Daphnia* and also inbred strains of rats; effects of introducing embryonic fluid into older animals.
- 15.10 Relation of cellular capacities to de-differentiate and re-differentiate to cellular age.
- 15.11 The rate of metabolism and oxidation-reduction potentials of tissues in relation to age and the catalytic components of aging cells.
- 15.12 Observations concerning the mechanisms regulating growth; gradual decrease in cellular assimilative capacities with age associated with gradual increase in the concentrations of nutriments in the blood stream of salamanders.
- 15.13 Effect of "rate of living" upon longevity and character and rate of senescent changes, studied in rats with experimentally raised and/or depressed basal metabolism.
- 15.14 Study of increasing metabolic response to thyroxin in rats of increasing age.
- 15.15 Effects of heat and X-ray radiation on tissues in relation to age.
- 15.16 Study of the continuous growth of teeth and facial skeleton in rats, monkeys, and man by vital staining with alizarine red; assessment of physiologic age by these data.
- 15.17 Statistical analysis of certain constitutional factors in determination of longevity.

16. Anatomy

- 16.1 Comprehensive study of normal histology and histochemistry of the skin of man in relation to age; long term program of detailed observations.

- 16.2 Study of hydration of the skin in relation to age as measured by electrical resistance.
- 16.3 Histologic study of human ovaries from patients between 40 and 50 years; attempt at defining normal in relation to age.
- 16.4 Histologic changes in normal dogs as observed from fetal life to senility. (Two separate studies)
- 16.5 Observations upon changes in rate and character of repair following injury in relation to age; study of compensatory renal growth in rats.
- 16.6 Histologic changes, particularly in relation to elastic tissue and calcification, in two groups of senescent rats: (1) normal control rats on adequate diet and (2) rats whose growth has been retarded and longevity increased by diets calorically deficient.
- 16.7 Histopathologic study senescent tissues, particularly of rats.
- 16.8 Study of relation of age to hemopoietic responses in mice of a leucemic strain.
- 16.9 Histology of the human pineal gland in relation to age.
- 16.10 Histologic changes in the cerebral cortex and cerebellum with aging; study of the Purkinji cells, Nissl substance and Golgi apparatus in human and rat brains. (Two separate studies, one extensive, the other projected.)
- 16.11 Histologic changes in dorsal root ganglia in relation to age in man.
- 16.12 Study of cartilage by histologic methods and application of Warburg technique at various ages.

- 16.13 Study of histologic changes in relation to age in normal inbred strain of mice. (Two separate studies)
- 16.14 Study of histologic changes in tendons and ligaments in man after the second decade.
- 16.15 Roentgenographic study of structural changes in skull and facial skeleton with aging in man, monkeys and rats.
- 16.16 Histochemical study of carbohydrate metabolism of the liver, pancreas and bowel in experimental animals in relation to age.
- 16.17 Histologic study of changes in bone structure in relation to age. (Two separate studies.)
- 16.18 Study of the histology of the pituitary gland in relation to age in chickens (changes with age resemble those observed in young castrates).

17. Biochemistry

- 17.1 Extensive study of effects of specific amino acids upon growth, development, differentiation and senescence in some twenty species.
- 17.2 Study of oxygen deficit in senile; methods unstated.
- 17.3 Study of colloid changes in relation to age; effect upon cell membranes.
- 17.4 Analytical study of changes in tissue electrolytes in relation to age.
- 17.5 Analytical study of lipoid content of muscle in relation to age.
- 17.6 Analytical study of collagen and other intercellular materials in relation to age.

- 17.7 Study of water balance and equilibria between tissue and blood water by photo-electric colorimetric methods in relation to age in man.
- 17.8 Analytical study of cholesterol concentrations in the blood in relation to the etiology of arteriosclerosis.
- 17.9 Tissue water studied in tissue cultures of various ages.
- 17.10 Analytical study of electrolytic ratios in animal sera in relation to age.
- 17.11 Hydration of cutaneous tissues in relation to age, studied by electrical resistance measurements.
- 17.12 Biochemical study of local chemical factors involved in calcification.

18. Physiology

- 18.1 Study of syndrome resembling premature senescence induced by hypophysectomy in rats.
- 18.2 Study of senescence accelerated by cold environment and increased metabolism.
- 18.3 Functional studies of physiologic changes produced by induced hypothermia.
- 18.4 Projected study of need for sleep in relation to age.
- 18.5 Study of changes in reactivity of structures in embryo and after puberty; responses to hormonal stimulation.
- 18.6 Relation of age to concentration of hydrochloric acid in the gastric juice.
- 18.7 Study of distribution of fluid in muscles of dogs with arterial hypertension induced by experimental hydro-nephrosis, with special emphasis of the role of potassium in the distribution of edema fluid.

- 18.8 Study of factors involved in cardiac hypertrophy and work capacity in relation to age.
- 18.9 Study of the reactivity of the sympathetic nervous system, the adrenal glands, and the vagus nerve to the secretion of insulin in relation to age.
- 18.10 Study of fluid balance and blood volume in relation to age and the so-called degenerative diseases.
- 18.11 Studies of arterial degeneration in salmon in relation to age and endocrine exhaustion.
- 18.12 Assay of pituitary hormones in relation to age and prostatic disease.
- 18.13 Projected study of the role of the adrenal glands in carbohydrate, protein and fat metabolism and electrolytic balance in relation to age.
- 18.14 Study of pulse rate, and metabolic rate in relation to age in retarded growth rats with delayed senility as compared with normal controls. (See 16.6 and 110.9)
- 18.15 Study of changes in metabolic rate in pigeons and doves in relation to age; effects of age on hormone changes of the reproductive cycles of female birds.
- 18.16 Study of effects of age upon metabolism of rats; adults apparently constant in their protein requirements, but immature and senile rats vary greatly in requirements.

19. Pharmacology and Toxicology

- 19.1 Study of differences in effects of drugs as related to age and investigation of possible application of such criteria to the measurement of physiologic age.
- 19.2 Library search for past work on relation of age to pharmacodynamic response to various drugs.

- 19.3 Extensive experimental investigation role of age in pharmacologic response to various drugs in rats.
 - 19.4 Study of effects of variable intakes of lead arsenate upon rat longevity and the character and extent of lead storage in relation to age.
 - 19.5 Study of variable intakes of fluorine in altering rat longevity and of fluorine storage in relation to age.
110. Nutrition (includes clinical studies)
- 110.1 Study of effects of feeding specific amino acids on growth, development, differentiation and senescence in over twenty species experimental animals.
 - 110.2 Study of effects of different levels of calcium feeding upon longevity and health of laboratory animals, controlled by analytical studies of the tissues. (Two separate studies)
 - 110.3 Study of longevity in relation to environmental temperature and total metabolic requirements; temperatures about 90°F. throughout life span of mice retard growth, lower metabolic consumption of foods and increase longevity.
 - 110.4 Study of incidence and rate of growth of breast cancer in inbred strain of mice kept in high environmental temperatures throughout their life span; retardation in development of cancer.
 - 110.5 Study of thiamin and pantothenic acid requirements under condition of lowered metabolism of mice kept at higher environmental temperatures in relation to age.
 - 110.6 Study of the effects of obesity upon longevity in rats.

- 110.7 Study of the effects of varying protein intake upon longevity in rats.
- 110.8 Projected study of the effects of certain inorganic constituents of the diet upon longevity in rats.
- 110.9 Extensive study of the effects of retarded growth in youth upon longevity, rate and character of senescence and structural changes in rats.
- 110.10 Study of relation of protein intake upon rate and character of regeneration and the protective action of proteins and certain specific amino acids against noxa.
- 110.11 Relation of fat deposition to aging in albino rats.
- 110.12 Projected application of electrophoresis and ultracentrifuge to study of relative distribution of blood proteins in relation to age.
- 110.13 Study of the effects of diet upon experimental renal insufficiency in white rats.
- 110.14 Study of the food getting habits and spontaneous selection of foods in rats in relation to age; observation of the defects in aged rats in relation to their feeding in youth.
- 110.15 Influence of nutrition upon the longevity of certain insects.
- 110.16 Study of the relation of aging to deficiency in "filtrate factors" in vitamin B complex (anti-gray hair vitamin). (Two separate studies)
- 110.17 Study of cholesterol metabolism in aged rats and guinea pigs with particular reference to hepatic changes.
- 110.18 Clinical application experimental studies with specific amino acids. (See 110.1)

- 110.19 Study of effects of varied protein and fat intake and of obesity in dogs with experimental arterial hypertension.
- 110.20 Study of relation of achylia gastrica to low calcium absorption and poor healing of fractures in the aged.
- 110.21 Hypovitaminosis as a factor in psychiatric disorders of the aged. (Three separate studies)
- 110.22 Study of vitamin C requirements of man as effected by age.
- 110.23 Clinical studies of scurvy among elderly persons.
- 110.24 Clinical study of arteriosclerotic heart disease in patients near 60 years old in relation to past dietary habits and present vitamin status, as determined by analytical determinations.
- 110.25 Application of photometer tests to study relation of age to vitamin A deficiency.
- 110.26 Clinical study relation exogenous obesity to juvenile and late forms diabetes mellitus.
- 110.27 Clinical study of efficacy in fat absorption in relation to age.
- 110.28 Clinical study of the relation of vitamin B complex deficiencies and functional digestive disturbances, with assays of blood vitamin content.
- 110.29 Clinical study of effects of optimum (?) calcium and vitamin intake in increasing blood supply to the extremities in peripheral vascular disease.
- 110.30 Projected clinical and experimental study of lipid metabolism and dietary intake in relation to arteriosclerosis.
- 110.31 Projected study of role of vitamin B complex in hepatic cirrhosis.

2. Clinical Investigations of Aging; Normal and Abnormal

21. Clinical Functional Evaluation

- 21.1 Physiologic and psychologic testing of effects of fatigue in relation to age.
- 21.2 Periodic physical examination employees with correlation of changes with age. (Several separate studies)
- 21.3 Study of changes of lung volume with age.
- 21.4 Study of changes induced by aging by application of clinical pulmonary function tests repeatedly over several years.
- 21.5 Determination of variation in normal blood sedimentation rate in relation to age.
- 21.6 Determination of variations in normal arterial tension in the aged.
- 21.7 Determination of variations in normal vital capacity in relation to age.
- 21.8 Study of normal hematologic standards for aged individuals.
- 21.9 Study of effects of age upon duration of immunity with standardized vaccination; study of effects of age upon the efficiency of antibody production in experimental animals (mammals).

22. Insurance Medicine

- 22.1 Statistical analysis causes of death at various ages.
- 22.2 Actuarial study relation body weight to longevity.
- 22.3 Statistical study role of heredity in human longevity.

23. Industrial Medicine

- 23.1 Measurement of abilities of several types in relation to age to assist in proper placement of aging employees.
- 23.2 Projected study of production output at various age levels in different occupations.
- 23.3 Critical study of data derived from annual periodic examinations of older employees. (Several separate investigations.)
- 23.4 Study of the ability of cardiovascular patients to work; correlation of type of employment to circulatory status with controlled follow-up studies.
- 23.5 Statistical study of age factor in employability.

24. Surgical Geriatrics

- 24.1 Clinical studies of special problems of surgical care of the aged with re-evaluation of surgical risk in relation to age. (Three separate clinical groups.)

25. Medical Geriatrics

- 25.1 Development of geriatric outpatient clinics with general geriatric clinical research in mind. (Three clinics)
- 25.2 Study of continuous clinical histories throughout life-span of individuals; projected continuation of similar study over several generations.
- 25.3 Hospital investigations of geriatric aspects of arteriosclerosis, hepatic cirrhosis, arterial hypertensive disease, arthropathies and the role of avitaminosis in chronic disease.
- 25.4 Study of neurologic functional changes attributable to age with attempt at standardization for ultimate mensuration of physiologic age.

26. Cardiovascular-Renal Disease

- 26.1 Clinical study of the ability of cardiovascular-renal disease patients to work and correlation of types of most suitable employment with type of disability and age.
- 26.2 Study of factors involved in cardiac hypertrophy; work capacity of the heart in relation to age.
- 26.3 Clinical study 100 cases arteriosclerotic heart disease in patients 60 years old or more in relation to vitamin status.
- 26.4 Biometric study of the records of several thousand cardiac patients 40 years old in 1915, carried up to date to age 65 in 1940.
- 26.5 Correlation of electrocardiographic findings with autopsy observations (many discrepancies being elicited).
- 26.6 Study of electrocardiographic findings in apparently normal men under varying stress conditions, with consideration of the factor of age.
- 26.7 Extension of studies into electrocardiographic findings in relation to specific cardiac lesions and age. (Several similar independent studies.)
- 26.8 Projected study of lipid content of diet and lipid metabolism in arteriosclerosis.
- 26.9 Experimental production arteriosclerosis with organ extracts; search for chemistry of active agents and analysis of data to reveal relation of age to vulnerability.
- 26.10 Clinical evaluation of methods employed in the diagnosis of peripheral vascular disease. (Three independent studies.)
- 26.11 Clinical study of the incidence of arteriosclerosis of the leg vessels in workers classified by occupation in relation to walking, standing and sitting.

- 26.12 Comparative evaluation various methods of therapy in arteriosclerosis obliterans: pressure-suction boot, oscillating bed, heat and the like.
- 26.13 Study of the changes in concentrations of chemical constituents of the blood in peripheral vascular disease.
- 26.14 Biochemical study of blood serum in atherosclerosis with attempt at isolation of accelerating and retarding substances.
- 26.15 Clinical study of the role of myxedema as an etiologic factor in arteriosclerosis.
- 26.16 Clinical and biochemical study of relation of lipocortic hormone to human atherosclerosis as seen in late diabetes mellitus and also to experimental arteriosclerosis in dogs.
- 26.17 Experimental studies of arterial degeneration in salmon in relation to endocrine exhaustion and age.
- 26.18 Clinical study of the role of tobacco in the etiology and/or pathogenesis of peripheral vascular diseases.
- 26.19 Experimental atherosclerosis in rabbits induced by high cholesterol diets; evaluation of pancreatic extracts in retarding development of the atherosclerosis.
- 26.20 Biochemical and pathologic studies into the role of cholesterol in the etiology and/or pathogenesis of arteriosclerosis. (Several independent investigations.)
- 26.21 Study of the solubility and biochemistry of sclerotic plaques from human blood vessels.
- 26.22 Clinical study of the effects of hormone therapy (pancreatic extracts and testosterone) upon the peripheral circulation of arteriosclerotic patients.

- 26.23 Clinical study of the effects of liberal calcium and vitamin intake upon the circulation of the extremities in elderly arteriosclerotic patients.
- 26.24 Projected study of the arterial and tissue elasticity in relation to age.
- 26.25 Pathologic study of the role of vascular disease in central nervous system changes found in old age.
- 26.26 Pathologic study of arteriosclerosis as observed in "wild" animals in zoologic gardens.
- 26.27 Histologic study of the vascular system.
- 26.28 Study of the pathology and vascular metabolism in arteriosclerosis.
- 26.29 Chemical and pathological study of experimental arteriosclerosis, including consideration of the influence of age upon vulnerability of the vascular structures to active injurious agents.
- 26.30 Clinical study of the natural history of hypertensive arterial disease; thorough clinical study of young hypertensive patients at least annually.
- 26.31 Clinical study of the physiology of the peripheral circulation as hypertensive disease progresses, including particularly photographs of retinæ and study of the blood flow in the extremities.
- 26.32 Pathologic investigation of the renal arteries in hypertensive arterial disease in 1000 cases, with projected extension of investigation of about 3000 more cases.
- 26.33 Experimental study of the mechanisms of hypertensive disease. (Several independent investigations.)
- 26.34 Study of the pulse volume in fingers in health at various ages, and in arteriosclerotic and hypertensive patients, by means of a photoelectric plethysmograph.

- 26.35 Clinical and experimental study of the role of the sympathetic nervous system in maintaining the peripheral circulation, with consideration of the effects of aging upon these homeostatic mechanisms.
- 26.36 Clinical study of methods of detection of pre-hypertensive states.
- 26.37 Clinical and statistical study of the factor of heredity in hypertensive disease.
- 26.38 Projected study of the role of heredity in altering vulnerability to vascular injury in experimentally induced hypertension in animals.
- 26.39 Clinical and experimental studies of the role of pressor substances of renal origin in the etiology and pathogenesis of hypertensive arterial disease. (Eight independent investigations.)
- 26.40 Study of the effects of varied protein and fat intake, and of obesity, upon the course of experimentally induced hypertension in dogs.
- 26.41 Clinical study of the efficacy of bromide sedation in hypertensive disease; (confirmation of other clinical studies reported in 1922).
- 26.42 Clinical study of the efficacy of surgical removal of thoracic and lumbar sympathetic chains and of splanchnic nerve resection in hypertensive disease.
- 26.43 Experimental study of the role of the carotid sinus in experimental induced hypertension in dogs.
- 26.44 Proposed clinical and pathological study of the course of chronic nephritis, with correlated evaluation of the renal functional capacity in relation to necropsy pathologic changes.

- 26.45 Pathological study of the changes in renal structure and function occurring with aging and compensatory growth following injury.
- 26.46 Projected statistical and biochemical study of tolerance to toxins, hemorrhage and anoxia in relation to age.
- 26.47 Clinical and pathologic study of renal changes occurring with aging.
- 26.48 Clinical study of changes in renal functional capacity in relation to age.
- 26.49 Experimental and clinical search for a new clinical renal function test sufficiently sensitive to detect very early depreciation of renal reserve capacity.
- 26.50 Study of tissue and blood water balance in renal disease by photoelectric colorimetry.
- 26.51 Clinical analyses of the physiologic mechanisms of the symptoms of renal disease.
- 26.52 Experimental study of the effects of various diets upon experimentally induced renal insufficiency in white rats.
- 26.53 Clinical study of the renal ability to excrete uric acid in relation to age, gout and/or known renal disease. (Three independent investigations.)

27. Endocrine Disorders

- 27.1 Projected clinical study of the role of the adrenals in maintaining electrolytic equilibrium and in carbohydrate, protein and fat metabolism.
- 27.2 Experimental study of adrenal functional activity in thyroid disease, hypertensive disease and various metabolic disorders, correlated with a pathologic study of adrenal degeneration and regeneration as seen in clinical material.

- 27.3 Pathologic study of the relation of changes in the adrenal cortex to hypertensive disease.
- 27.4 Study of the lipid metabolizing fraction of the anterior pituitary hormones in relation to arteriosclerosis, obesity and aging.
- 27.5 Study of the phenomenon of premature senescence in hypophysectomized puppies.
- 27.6 Parathyroid function assays correlated to age and in relation to bone atrophy in senescence.
- 27.7 Assays of thyroid function throughout life span.
- 27.8 Study of various hormone titers and the structural changes in the endocrine glands at the climacteric.
- 27.9 Experimental studies of pituitary and ovarian hormones during the climacteric in the rat.
- 27.10 Study of the pathology and therapy of atrophic conditions of the vulva and vagina in senescent women.
- 27.11 Clinical study of hormone titers and excretion in relation to the climacteric and aging. (Three or more independent investigations.)
- 27.12 Study of relation of estrogens to myeloid aplasia.
- 27.13 Pathologic study of non-sexual organs in the period of the menopause; relation of gonadal secretions to rate of senescence.
- 27.14 Clinical studies of the control of menopausal symptoms by therapy with estrogenic preparations. (Several studies.)
- 27.15 Projected experimental study of the endocrine factors in aging of the genital organs in mice.
- 27.16 Histologic study of ovaries from women between 40 and 50 years old.

- 27.17 Studies of methods for assaying estrogens by mitosis counts on endometrial tissue from immature female rats.
- 27.18 Experimental study of blocking effects of androgens upon estrogenic activity in rabbits.
- 27.19 Extensive experimental study of the influence of sex hormones upon cancer growth, with consideration of factor of age in relation to pharmacodynamics.
- 27.20 Experimental study of the effects of estrogens upon bones and ossification in relation to age.
- 27.21 Experimental study of the apparent causation of renal hypertrophy by androgens.
- 27.22 Experimental study of inhibition of hair grown by estrogens in dogs.
- 27.23 Study of the decline in fertility with age in horses, cattle, sheep, swine and fowls.
- 27.24 Study of the role of hormones in the prolongation of lactation in aging dairy cattle.
- 27.25 Clinical study of the relation of previous acute and preventable diseases to the etiology of diabetes mellitus, with attempt to distinguish between the effects of normal senescence and those of cumulative injuries.
- 27.26 Clinical study of nutritional status in diabetes mellitus in senile individuals; geriatric diabetic metabolism.
- 27.27 Pathologic review of the complications of diabetes mellitus in relation to age; study of 500 autopsy examinations made upon diabetic subjects.

- 27.28 Clinical study of the physiology of insulin in older diabetic patients.
- 27.29 Projected clinical study of the effects of testosterone upon the course of diabetes mellitus in elderly patients.
- 27.30 Extensive clinical study in differentiating "juvenile" and "late" diabetes mellitus with emphasis upon the role of obesity in the etiology of the latter.
- 27.31 Clinical analytic study of the blood content of acetone in relation to age and state of carbohydrate metabolism.
- 27.32 Biochemical study of hepatic metabolism in diabetes mellitus with analyses for glucose, lactic acid, acetone bodies and lipids in the hepatic and portal veins.

28. Arthropathies

- 28.1 Statistical and clinical studies of the hereditary factors of gout.
- 28.2 Clinical study of the relation of foci of infection to the arthropathies and to premature senescence.
- 28.3 Clinical and experimental study of the nutrition and metabolism of articular cartilage in relation to age.
- 28.4 Clinical pathologic study of the degenerative changes in bone and cartilage occurring with age, with particular emphasis upon the circulatory changes and the influences of obesity.
- 28.5 Histologic study of nervous tissue in joints in attempt to correlate depreciation of proprioceptive mechanism occurring with aging with the etiology of senile hypertrophic arthritis.

29. Clinical Studies in Neurology, Psychology, and Psychiatry Relating to Aging.

- 29.1 Study of the utilization of oxygen by cerebral tissues in relation to age.
- 29.2 Study of the cerebral circulation time and changes in arterial tension related to posture at various ages.
- 29.3 Histologic changes in the cerebral cortex and cerebellum occurring with aging; study of changes in Purkinji cells, Nissl substance and Golgi apparatus.
- 29.4 Histologic study of the postnatal development of the human cortex cerebri.
- 29.5 Pathologic studies of vascular changes in the brain in relation to age. (Three independent studies involving material from over 26,000 postmortem examinations.)
- 29.6 Histologic study of the morphology of the brain in senile as contrasted with pre-senile psychoses.
- 29.7 Pathologic study of the brain and spinal cord in relation to symptomatology in neurologic conditions among the aged.
- 29.8 Study of the chemical characteristics of the spinal fluid in senile psychoses and arteriosclerotic dementia. (Two independent investigations.)
- 29.9 Histopathologic study of the central nervous system in dehydration in the aged.
- 29.10 Psychologic study of intelligence patterns in the aged, especially regarding the capability of willing.
- 29.11 Psychometric study of memory function and vocabulary function in persons from 20 to 90 years old, directed toward obtaining norms in relation to age.

- 29.12 Psychologic studies with groups of aged persons. (Several independent investigations.)
- 29.13 Projected study of differential functional changes occurring with aging.
- 29.14 Statistical (historical) study of age in relation to peak performance in various lines of endeavor, such as music, literature, and sports.
- 29.15 Study of memory defects in the aged.
- 29.16 Study of language changes occurring in aging.
- 29.17 Study of the depreciation of sensory-motor and psychological capacities with age.
- 29.18 Analysis of social and psychological problems of patients over 70 years old, leading to admission to mental hospitals.
- 29.19 Clinical studies of the etiology of the senile psychoses. (Several independent investigations.)
- 29.20 Study of the lipoid metabolism and neuropathology of the aged.
- 29.21 Clinical study of the relationship of hypertensive arterial disease to mental disease.
- 29.22 Study of the role of vitamin deficiency in the etiology of mental disorders of the aged. (Several independent investigations.)
- 29.23 Clinical study of toxic psychoses of elderly patients in relation to arteriosclerotic psychoses.
- 29.24 Clinical study of the relation of involutional melancholia to organic evidences of senescence.

- 29.25 Clinical study of relation of nocturnal confusion in the aged to the oxygen supply to the brain.
- 29.26 Clinical study of the psychic changes induced in the senile by oxygen inhalation therapy.
- 29.27 Study of the response of cerebral blood vessels to vasodilator substances, particularly histamine, in relation to age.
- 29.28 Study of the response of the cerebral circulation to aminophyllin administered intravenously to patients with senile dementia.
- 29.29 Pathologic study of the relation of Pick's Lobar atrophy to senility.
- 210. Clinical Studies into Geriatric Gastroenterology.
 - 210.1 Projected roentgenographic study of gastric motility in elderly persons.
 - 210.2 Extensive clinical study of atrophic gastritis and search for evidence of possible sequence relationship between atrophic gastritis and gastric cancer; projected experimental production of atrophic gastritis in animals by roentgen radiation with both functional (secretory) and histologic control study.
 - 210.3 Clinical study of the relation of diverticulitis of the colon and/or sigmoid to anatomic changes of senescence.
- 211. Geriatric Ophthalmology.
 - 211.1 Projected study of corneal changes occurring with senescence.
 - 211.2 Study of diminution of light sensitivity in relation to age, correlated with studies in optimum illumination.
 - 211.3 Statistical and clinical study of visual acuity and depth perception in relation to age in industrial medicine.

- 211.4 Clinical study of ophthalmic lesions associated with focal infections and relation to the processes of senescence.
- 211.5 Clinical study correlating systemic disease and age with glaucoma and cataract.
- 211.6 Experimental study of the changes in metabolism in the lens with age; both in normal lenses and in those presenting senile cataracts.

212. Genito-Urinary Geriatrics.

- 212.1 Biochemical investigation of prostatic involution; assay of androgenic hormones in the urine of patients with prostatic hypertrophy.
- 212.2 Experimental study of the prostatic response to hormone administration. (Two independent investigations.)

213. Cancer in Relation to Aging. (Obviously a most incomplete list, as no special effort was made to include all cancer research. Reports of these studies elicited upon inquiry concerning work on aging.)

- 213.1 Statistical study of the relationship of cancer incidence to age by separate analyses of data concerning specific types and locations of the malignant neoplasms.
- 213.2 Experimental study of cancer incidence in inbred cancer-bearing strain of mice as effected by environmental temperature and rate of senescence.
- 213.3 Clinical study of gastroscopic findings, gastric juice analyses, and other clinical data in atrophic gastritis in search of evidence of possible etiologic role of atrophic gastritis in gastric cancer.
- 213.4 Pathologic study of the morphology of polypi of the colon in relation to age and colonic neoplasms.
- 213.5 Pathologic study of skin tumors in relation

- 213.6 Pathologic study of mammary involutional changes occurring with aging in relation to mammary cancer.
- 213.7 Histologic study of cytoplasmic changes in young normal, senile normal and malignant cells induced by radiation of various types.
- 213.8 Experimental study of hormone assays in relation to appearance of spontaneous cancers in rats and mice. (Two independent investigations.)
- 213.9 Biochemical comparison of enzyme systems of cancer and normal cells, with consideration of variation in normal in relation to age.
- 213.10 Study of growth retarding (maturation stimulating) substances extracted from cancer tissue and normal tissues from animals of various ages.
- 213.11 Experimental and biochemical study of induction of cancer by carcinogenic agents. (Many independent investigations, but only a very few giving consideration to the factor of age.)
- 213.12 Extensive study of the effects of specific amino acids upon growth, development, differentiation in over 20 species animals, with consideration of tissue age in data correlation.
- 213.13 Pathologic and experimental study of leucosis in poultry in relation to age.

3. Socio-economic Problems.

31. Social Science Studies.

- 31.1 Extensive and comprehensive statistical analyses population changes by U. S. Bureau of the Census.
- 31.2 Clinical study of the health of 100 persons before and after retirement; evaluation of physiologic consequences of retirement.

- 31.3 Sociologic study of social adjustments of 50 elderly rural individuals contrasted to a similar urban group.
- 31.4 Statistical study of age changes in populations and the socio-economic consequences. (Study discontinued.)
- 31.5 Surveys of chronic illness in relation to age in two large cities.
- 31.6 Projected study of productive output at various age levels in different occupations.
- 31.7 Projected study by social service worker of placement problems of older people.
- 31.8 Clinical study of employability of physically handicapped persons, including those handicapped by reason of age.

Comment

Though the survey has revealed a considerable number of active investigations into problems of gerontology, it is notable that many of these are projected studies and represent wishful thinking rather than basic or fundamental researches. The studies actually underway are widely scattered, both geographically and scientifically, for there are a few serious students in most of the scientific disciplines which are applicable to the study of aging. Certain areas of the field are being woefully neglected; in others some over-emphasis has encouraged unnecessary duplication of effort. It would be profitless to attempt a detailed analysis of the pattern of present studies. Certain

comments concerning the more obvious discrepancies in orchestration are, however, justified.

In the first division of gerontology, concerned with the biology of senescence, there is great and urgent need for far more extensive investigations. The solution of many of the clinical problems of geriatrics and thus intelligent attack upon the pressing socio-economic questions hinge largely upon an increase in precise factual information regarding just what senescence is and does. (12) There is need for thorough and detailed studies into the structural changes consequent to senescence; morphologic, cytologic and histochemical investigations of tissues from animals or human beings of various ages should be fostered and encouraged, for it is necessary to establish a baseline of structural normality in relation to age before attempting identification of the factors which retard or accelerate the processes of senescence. A few such investigations are underway, but they are far too few. It must not be forgotten that researches of this nature are time consuming, laborious and hardly dramatic. Yet such knowledge is the foundation upon which the science must rest. (13)

Neglected also are studies into the physiologic and biochemical changes that are a part of aging. Particularly pertinent are investigations of changes in the

mechanisms and efficiency of the equilibratory processes in relation to age and the mensuration of reserve capacities. The internal environment of the body must be maintained within narrow limits; resistance to disease is largely a question of physiologic responses to influences tending to disturb such homeostatic equilibrium. Quantitative evaluation of the various mechanisms involved in relation to age is as important as studies of qualitative alterations. Such studies are preliminary requisites to the development of clinical methods for the measurement of physiologic age in men and women and, thus, to more precise procedures for the mensuration of health at any age.

Biochemical studies of changes in the processes of cellular oxidation and reduction, enzymatic activity, metabolism electrolytic balance, lipid and protein distribution in relation to age are conspicuously lacking in the list of investigations elicited. It is impossible for the few scientists now concerned with these problems to advance knowledge rapidly enough so that clinical medicine may be forearmed for proper health maintenance of the quickly increasing millions of elderly in the population.

The role of nutritional factors in accelerating or retarding the aging processes is badly in need of greatly extended study. Very little indeed is known anent the body's requirements for vitamins in relation to age. It is highly

possible that these may fluctuate widely. We now know almost nothing of the relative efficiency of vitamin absorption at various ages. With diminished efficiency of absorption a larger oral intake may be necessary to insure an adequate supply even though the body's requirements remain unaltered. These two factors must be considered as independent variables. It is obvious that the recent trend in research into the problems of nutrition has become illogically asymmetric; there is a tremendous concentration of effort upon problems dealing with specific deficiencies and an almost complete absence of interest in the relationships between excessive consumption of calories, obesity and longevity. Of the many investigators in nutrition, there were found but two actively interested in the over-nutritional aspects of malnutrition, (14) despite the convincing and dramatic statistical evidence that overeating is the graver menace in the later years of life. (15) This unscientific over-emphasis of nutritional inadequacies and ignoring of the deleterious effects of nutritional excesses are even more conspicuous among the clinical studies of human nutrition.

In the second category of gerontology, clinical geriatrics, almost all research has been directed toward abnormal senescence, or the diseases whose incidence rises sharply after the meridian of life. There is a dearth of

interest in normal aging. Studies of methods of health evaluation, definition of criteria of normality in relation to age, and the development of procedures to measure physiologic age are conspicuous by their absence, with the exception of psychometric investigations. (16) The measurement of health is fraught with difficulty. Thus far no one has attempted to formulate an adequate minimum routine for diagnostic study to reveal the degree of health, nor has there been any suggestion of tentative standards in relation to age other than those relating to the arterial tension and basal metabolic rate. Arbitrary standards based upon chronologic age are wholly unsuitable. This has been repeatedly emphasized in pediatric literature and it is still more significant in geriatric practice, for the greater the duration of life the wider will be the fluctuations between physiologic and chronologic age. One logical approach to quantitation of biologic age is through the measurement of several reserve capacities; for example, the cardiac reserve, renal reserve, hematopoietic reserve, and hepatic functional reserve. No single observation can ever suffice, for aging does not proceed uniformly throughout the individual. Depletion of reserves occurs long before actual functional failure and must needs be detected and measured if preventive measures are to retard disability from functional failures.

Clinical medicine is slow to awaken to the potentialities of personal preventive geriatrics. (7) There are two kinds of preventive medicine, the impersonal, "wholesale" or public health approach, and the individual or "retail" form of prophylaxis. Pediatrics has applied both methods. The resulting improvement in the health of the young and in the reduction of infantile and juvenile mortality have been magnificent. Pediatrics advanced rapidly only after it was recognized that the child is not "the little man," but presented functional, nutritional, structural and immuninologic problems peculiar to infancy and childhood. A similar focus of attention upon the changes induced by normal senescence is necessary before preventive medicine for the later years of life becomes as effective as it can with the wiser application of existing knowledge. Thus far, preventive medicine for adults has been almost wholly limited to the "wholesale" or public health type of approach: institution and control of sanitation, enactment and enforcement of quarantine regulations, control of avoidable hazards of atmospheric contamination, and attempts at mass diagnosis of certain communicable diseases. Such methods are effective in the prevention of infective diseases, but are wholly inappropriate to prophylactic geriatrics. Preventive geriatrics must be applied individually and personally. With aging comes increasing

divergence from the mean and greater individual variation. Furthermore, the commoner diseases of middle and later life are largely endogenous and not infective. Individualization is the keystone to the arch of effective preventive medicine for the aging. Far more can be accomplished prophylactically for the aging from 40 to 60 years than for the truly senile or those already disabled by the chronic insidious and progressive disorders of geriatric practice. These disorders must be searched for individually if they are to be detected early enough to accomplish retardation or control by therapeutic means. Clinical medicine needs to be aroused from its apathy in this field of practice. The most encouraging sign elicited by the survey is that in many places industrial medicine is awakening to the potentialities of health maintenance activities for its valued personnel.

Clinical studies into the so-called degenerative diseases characteristic of later life are numerous and many are wisely conceived, thoroughly controlled, and conscientiously executed. There appears, however, to be some asymmetry in the placement of emphasis. Though cardiovascular-renal diseases account for more than three times the number of deaths than does cancer of all forms (17), the study of neoplastic diseases is receiving much more

financial support and popular attention. The present investigations into the etiology and pathogenesis of arteriosclerosis (18,19) are of the highest calibre and deserving of further financial encouragement. Investigations concerned with the etiology and mechanisms of hypertensive arterial disease greatly emphasize the role of pressor substances of renal origin. The dramatic and significant results of Goldblatt and his coworkers in 1934 (20) have caused some investigators to believe that extension of these studies will lead to finding a single or universal cause of hypertensive disease, whereas the disorder results from many causative factors and each instance is an individual problem. (21)

Worthy of special mention is the dearth of studies into disorders of the senile skin. Studies in genitourinary and gynecologic geriatrics appear to be almost wholly limited to investigations concerning the role of the sex hormones in relation to prostatic changes in men and the menopausal syndrome in women.

Research in the third and most urgent category of gerontology, the social and economic problems of the aging, was found to be almost nonexistent. Population studies by the U. S. Bureau of the Census (22), statistical compilations by the Bureau of Old Age and Survivors Insurance of the Social Security Board (23), and the studies of the National

Resources Committee (24) all emphasize the growing necessity for intelligent planning. But, with the exception of a very few small studies concerning employability of elderly persons, there are no serious efforts at fact finding to guide those hoping to solve these critical questions. Problems of adult education, employment, the treatment of chronic illness among the aging, custodial care for the senile and the questions raised by the immense pool of leisure time of the elderly are being almost totally ignored. There are distributed annually several hundreds of millions of dollars for old age assistance, but there is no appreciable expenditure in an effort to learn something of the specific needs of the elderly or of the changes in their capacities so that they might work effectively within their biologic limitation.

An Outline of Significant Problems in Gerontology

The survey reported above has revealed that there is little coordination or orchestration in scientific research in gerontology. As stated in the introductory paragraphs of this report, orchestration of research involves three preliminary procedures: 1) The orientation of the categories of thought involved; 2) inventory of present and projected studies; and 3) correlation of existing knowledge for the purpose of formulating a broad research program. The third and last of these procedures can be only suggestive; it would be utterly illogical and most unwise to attempt any

centralized planning or directed organization of scientific research in this or any field. Unhampered originality, imagination and specific curiosities of individual scientists are requisite for scientific advance; any regimentation of thought stifles these essential attributes. Each advance in knowledge brings forth many new questions and suggests divergent collateral avenues of approach. It is possible, however, to formulate a broad skeletal plan into which innumerable researches will fit like the pieces of a jig-saw puzzle and thus orient individual contributions to the solution of the whole.

The following tentative outline of problems in gerontology is thus intended only to be suggestive for a more organized consideration of the problems and to be of aid in orientation of studies. It is obviously by no means exhaustive. Particularly limited are the enumerated examples of possible specific research projects.

Outline of Problems in Gerontology

A. The Biology of Senescence

1. Structural changes

- 1.1 Gross changes in tissues with age
- 1.2 Histological changes in mammalian tissues
- 1.3 Gross changes in organs and systems

1.4 Histological changes in organs and systems

1.5 Structural changes in senescence in lower
forms of life

1.51 Examples: In protozoa
bacteria
plants
reptiles
amphibia, etc.

1.6 Histochemical changes in tissue composition

1.61 Electrolytic changes

1.62 Changes in water content and water
distribution within cells

1.63 Lipoid changes

1.631 Qualitative character of lipoids

1.632 Quantitative distribution of lipoids

1.7 Relating changes observed to

1.71 Types of tissue

1.72 Functional activity of tissue

1.73 Species animal

1.74 Age of animal

1.75 Phylogenetic age of tissue

2. Functional changes

2.1 Qualitative functional changes with "normal"
senescence

2.2 Quantitative functional changes in relation to age

2.3 Mensuration of function reserve capacities and
variation of these with aging

2.4 Mensuration of variability of "physiologic
constants"

2.41 Variation with aging

2.42 Inter-relationship between variation
of one with others

2.43 Examples: Thermostability
Water equilibrium
Pulse stability
Arterial tension
Chemical "constants"
(acid-base balance)

2.44 Qualitative and quantitative mensuration
of the "constants" with different ages

2.45 Study of changes in the homeostatic
mechanisms maintaining the equilibrium
of the "constants"

2.5 Pharmacologic and toxicologic changes with age

2.51 Quantitative and qualitative changes in
pharmacodynamics in relation to age

2.511 Correlation with species

2.512 Correlation with type of drug

2.513 Correlation with pharmacologic
response

2.52 Reaction at different ages to injury

2.521 Examples: Anoxemia
Drugs
Fatigue
Toxic gases and fumes
(industrial health
application)
Trauma
Altered environmental
temperatures
Nutritional injury

2.522 Tissue regeneration at different
ages, especially in relation to
growth stimulation (intimately
related to study of carcinogenic
agents).

3. Biochemical changes

3.1 Qualitative changes with advancing years

3.11 Inorganic constituents

3.12 Lipoid constituents

- 3.13 Protein constituents
- 3.14 Enzymatic constituents
- 3.15 Hormonal constituents
- 3.16 All other organic constituents
- 3.2 Quantitative changes (normal) with advancing age
 - 3.21 Inorganic constituents
 - 3.22 Lipoid constituents
 - 3.23 Protein constituents
 - 3.24 Enzymatic constituents
 - 3.25 Hormonal constituents
 - 3.26 All other organic constituents
- 3.3 Constancy of chemical constitution of body
- 3.4 Alterations in oxidation-reduction systems
- 4. Factors accelerating or retarding senescence
 - 4.1 Study of influence of heredity (statistical)
 - 4.2 Study of influence of diets
 - 4.21 To include
 - 4.211 Effects of specific deficiencies
 - 4.212 Effects of excesses
 - 4.22 Experimental diets to be applied during:
 - 4.221 Youth and growth period of life
 - 4.222 Middle period of life
 - 4.223 Senescent period

- 4.3 Study of effects of specific diseases (past)
upon longevity
 - 4.31 Statistical analysis of late (delayed)
effects of previous illnesses.
 - 4.32 Variation in severity of disease in
connection with age
- 4.4 Study of the effects of fatigue upon longevity
 - 4.41 Must include various sorts of fatigue
- 4.5 Study of effects of various chemical agents
(other than dietary)
 - 4.51 Illustrated by effects of specific
substance upon plant nutrition
 - 4.52 Endocrine imbalances
 - 4.53 Variation in the "physiologic constants"
 - 4.54 Age variation of toxicologic vulnerability
- 4.6 Study of the effects of physical environment
upon longevity

B. Clinical Problems (applied to man)

1. Objective: To aid in enabling man to continue
health and vigor and avoid premature senescence
rather than an attempt at prolonging the life span
into unusual and increasing periods.
2. Methods of Health Evaluation
 - 2.1 Appraisal of existing methods of health evaluation
 - 2.2 Development of new methods and new criteria of
health evaluation and determination of physiologic
age
 - 2.3 Application of such clinical studies to groups
advancing in age; to be carried out over a
period of years

NOTE: With particular emphasis on the depreciation
of functional reserve capacities and methods
of measuring these.

3. Determination of physiologic "constants" at various ages, with or without associated diseases.
 - 3.1 Variation of these with age
 - 3.2 Examples: Thermostability
Vital capacity
Water equilibrium
Vitamin metabolism
Arterial tension
Glucose metabolism
Acid-base homeostatis
 - 3.3 Study of the ease (or difficulty) with which these "constants" are altered at various ages, and changes in homeostatic mechanisms.
 - 3.4 Inter-relation of various "constants" with one another.
4. Disorders whose frequency increases with senescence
 - 4.1 Examples: Hypertensive arterial disease
Arteriosclerosis
Cerebral
Coronary
Systemic

Diabetes mellitus

Gout

Climacteric
Male
Female

Arthropathies

Cancer
 - 4.2 Problems involved with each of these include
 - 4.21 Etiology:
 - 4.211 Predisposing factors
 - 4.212 Provoking factors
 - 4.213 Perpetuating factors
 - 4.22 Pathogenesis
 - 4.23 Methods of earliest possible detection (clinical)

4.231 Potentiality

4.232 Early evidences of occult onset

4.24 Therapy

4.241 Prophylactic

4.242 Curative (etiologic)

4.243 Controlling (physiologic)

5. Changes in body responses to injury

5.1 Variation in vulnerability to toxic influences with advancing age -- toxicology

5.11 Variation in pharmacologic response to medication with advancing age

5.12 Variation in toxic effects drugs as well as other toxic substances

5.2 Variation of the mechanisms of defense to noxa

5.3 Changes in reactions to infection (immunologic changes with age)

5.4 Study of reaction to specific toxins and classification of those noxious substances for which vulnerability increases with age in contrast with those which become less injurious as age increases

6. Statistical analysis of effects of previous experiences upon physiologic age, reparative processes of the body, homeostatic mechanisms, physiologic constants and the like

6.1 Analysis re previous illnesses

6.2 Analysis re previous nutrition

6.3 Analysis re previous occupations

6.4 Analysis re various other vicissitudes of existence

C. Mental Changes with Aging

1. "Normal" changes with senescence

1.1 Qualitative studies

1.2 Quantitative studies

1.3 Two modes of approach: Studies of large groups of individuals at various ages and study of a relatively smaller number of persons repeatedly over a period of years as they age

2. Differentiate emotional and intellectual changes

2.1 Intellectual changes studied from viewpoint of learning the more appropriate placement of older workers

Must consider: Speed of reaction
Logic
Thoroughness
Endurance at mental concentration
Accuracy, etc.

2.2 Clinical psychotherapeutic studies

2.3 Neuroses in aged

2.4 Psychosomatic studies

3. Educational problems (overlap greatly with "D")

3.1 At present there is no educational preparation for senescence

3.2 Cooperation with educational organizations anent adult education and especially education of present generation of children in anticipation of their much greater life expectancy

3.3 Investment of leisure

3.4 Educational methods as applied to adult and aging individuals.

D. Sociologic Problems

1. Economic

- 1.1 Changes in population age spread
- 1.2 Effect of this upon migration (climate)
- 1.3 Earnings and occupations with senescence
- 1.4 Age and intellectual work capacity
- 1.5 Taxation, production and assistance in relation to advancing age
- 1.6 Studies in effective placement of older workers (considering the value to the community)

2. Adult educational problems

3. Family problems

- 3.1 Economic aspects
- 3.2 Psychological aspects; element of mutual respect
- 3.3 Utilization of the assets of aged in the home
- 3.4 Determination of the optimum environment for happiness in old age, considering sense of usefulness as well as purely economic "security"

Conclusion

It is hoped that this report of a survey of present and projected research studies into the problems of aging in the United States, the critical analysis of the data derived, the orientation of the science of gerontology, and the presentation of a tentative skeletal outline of a broad program of future research may serve the following purposes:-

- 1) Assist in increasing cooperation between investigators interested in related problems though applying widely divergent disciplines.
- 2) Emphasize the urgent need for greatly augmented support to significant studies into the phenomena of senescence.
- 3) Stimulate interest, curiosity, and new research endeavors among scientists.
- 4) Assist in the formulation of future research programs.

The need to know far more about aging and the aged is becoming increasingly critical. The conspicuous shifts in population structure can no longer be ignored. There is much work to be done before science can accumulate the factual data necessary for intelligent solution of the immense and pressing social problems.

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